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MANAGEMENT OF ALCOHOL WITHDRAWAL SYNDROME: A SYSTEMATIC REVIEW

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Abstract

A clinical condition known as Alcohol Withdrawal Syndrome (AWS) develops in people with chronic alcohol use disorder (AUD) when their alcohol consumption is reduced or stopped. From minor discomfort to serious, life-threatening complications like seizures and delirium tremens, the syndrome can present with a wide range of symptoms. AWS's pathophysiology, clinical manifestations, diagnostic techniques, management approaches, and prevention are all intended to be thoroughly covered in this review. It also looks at new developments in therapy and how tailored care can help patients get better results.

Keywords: Alcohol use disorder (AUD), etiology, epidemiology, management, disorder.

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Introduction

Heavy drinking and binge drinking are included in the intervening category, which is referred to as risky drinking.AUD is a long-term condition that affects the patient's health, relationships, and mental state. Additionally, AUD has a major effect on the healthcare system, accounting for 7.4% of ER visits and more than 200,000 hospitalizations annually [1]. A third of patients admitted to hospital intensive care units (ICUs) and up to 42% of patients admitted to general hospitals are thought to have AUD. About 8% of hospitalized AUD inpatients experience alcohol withdrawal syndrome (AWS), a well-known condition that happens after an abrupt, either intentional or unintentional, cessation of heavy or continuous drinking. Severe AWS often necessitates ICU treatment and more than doubles the length of stay. Epileptic seizures and/or delirium tremens (DT), which can occur in as many as 15% of AUD patients, are examples of complicated AWS. The mortality rate of delirious patients is similar to that of patients with severe malignant diseases, and they exhibit high rates of comorbidities [2-5].

Etiology

Susceptibility to alcohol use disorder is probably multifactorial, even though the precise etiology of the disorder is still unknown. Twin and adoption studies indicate that environmental factors account for the remaining 50% of the liability, with genetics accounting for about 50%. Although more research is required, it is likely that neurobiological and epigenetic adaptations contribute to the development of AUD [6-7].

Epidemiology

According to the 2022 National Survey on Drug Use and Health, 67.4% of people aged 18 and older reported using alcohol in the previous year, making it the most widely used drug in the US. Regarding risky drinking habits, 6.3% of people aged 18 and over reported heavy alcohol use, and 23.5% reported binge drinking in the previous month. The Substance Abuse and Mental Health Administration estimates that 29.5 million people aged 12 and older had AUD in 2022, making it the most common substance use disorder diagnosed in 2019 [8]. In addition to being a frequent reason for hospitalization, alcohol withdrawal syndrome is also frequently treated in patients who are admitted for other reasons. One in seventeen hospitalized veterans received treatment for alcohol withdrawal syndrome, according to a 2013 study of more than 450,000 hospital admissions.9

Pathophysiology of Alcohol Withdrawal Syndrome [10-12]

Long-term alcohol use alters the central nervous system (CNS) in neuroadaptive ways. Glutamate, the main excitatory neurotransmitter, and gamma-aminobutyric

acid (GABA), the main inhibitory neurotransmitter, are the two main neurotransmitter systems that are mainly impacted by alcohol.

1. **GABAergic System:** Long-term alcohol consumption increases GABAergic inhibition, which lowers CNS excitability. The body adjusts to prolonged alcohol use by lessening GABAergic neurotransmission and GABA receptor sensitivity.
2. **Glutamatergic System:** On the other hand, long-term alcohol consumption inhibits glutamate, which increases the quantity of NMDA (N-methyl-D-aspartate) receptors. Excitatory neurotransmission is overactive when alcohol consumption is abruptly decreased or stopped, which adds to the hyperexcitable state that is a hallmark of withdrawal.
   These excitatory and inhibitory systems become unbalanced when alcohol consumption is abruptly stopped, which can result in symptoms like anxiety, seizures, and tremors. Delirium tremens (DTs) or other potentially fatal consequences may arise from this dysregulation in extreme circumstances.

Clinical Features of Alcohol Withdrawal Syndrome13-16

AWS symptoms can vary greatly based on the degree of dependence, rate of alcohol reduction, age, co-occurring medical conditions, and psychiatric comorbidities of the individual. The symptoms can be categorized as mild, moderate, or severe and typically manifest 6 to 24 hours after the last drink.

1. **Mild Symptoms**
   - Irritability and anxiety,
   - Tremors, or unsteadiness
   - Sweating
   - Vomiting and nausea
   - Sleeplessness
2. **Moderate Symptoms**
   - Tachycardia, or fast heartbeat
   - High blood pressure, or hypertension.
   - Confusion and agitation
   - Depersonalization, or a sense of disassociation from the body
   - Having trouble focusing
3. **Severe Symptoms:**
   - Seizure
   - Delirium Tremens (DTs): marked by severe autonomic dysfunction (e.g., tachycardia, fever, and fluctuating blood pressure), confusion, disorientation, and hallucinations
   - Hallucinations, both visual and auditory
   - Elevated body temperature, or hyperthermia

The Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale is commonly used to quantify the severity of withdrawal symptoms and guide treatment. It assesses 10 symptoms: nausea/vomiting, tremor, paroxysmal sweats, anxiety, agitation, tactile disturbances, auditory disturbances, visual disturbances, headache, and orientation.

Table 1: Alcohol withdrawal syndrome findings.

Syndrome	Characteristics	Timeline
Initial withdrawal signs/symptoms	-Tachycardia, hypertension, increased body temperature, tremor*, insomnia, anxiety, nausea, vomiting, headache, diaphoresis, palpitations	6-8 hours after last drink
Alcohol hallucinations	-7%-8% of patients with AWS-Tactile hallucinations common, visual less likely-Auditory hallucinations possible (sometimes persecutory)-May present with tremors and other withdrawal symptoms, though some do not-Normal sensorium	12-24 hours after last drink
Withdrawal seizures	-Generalized tonic-clonic, though often isolated, short in duration, short postictal period-1/3 of patients with withdrawal seizures will progress to delirium tremens	12-48 hours after last drink
Delirium tremens	-5% of all patients undergoing AWS-Rapid-onset, fluctuating disturbance of attention and cognition plus alcohol withdrawal symptoms-Diagnosis requires autonomic instability	Begins 3 days after the appearance of AWS symptoms and lasts 1-8 days

AWS, alcohol withdrawal syndrome.

Diagnosis of Alcohol Withdrawal Syndrome

The diagnosis of AWS is primarily clinical, based on a history of alcohol use and the presence of withdrawal symptoms after cessation or reduction in alcohol intake. In some cases, laboratory tests may be used to rule out other conditions or to monitor complications, including:

Complete Blood Count (CBC)

To assess for signs of infection or anemia.

- **Liver Function Tests**
  Chronic alcohol use often leads to liver damage, and elevated liver enzymes may indicate liver dysfunction.
- **Electrolytes and Blood Glucose**
  To monitor for dehydration, hypoglycemia, or electrolyte imbalances.
- **Alcohol Blood Levels**
  In certain cases, alcohol levels may still be detectable in the bloodstream, which can help confirm alcohol use. If AWS is suspected, it is essential to differentiate it from other conditions that may present with similar symptoms, such as infections, metabolic disorders, or psychiatric disorders like panic attacks or anxiety [17].

Management of Alcohol Withdrawal Syndrome [18-21]

Pharmacological Interventions: Controlling symptoms and avoiding serious complications are the main goals of AWS treatment. Because of their GABAergic effects, which aid in reestablishing the central nervous system's equilibrium, benzodiazepines are the mainstay of pharmacologic therapy.

Benzodiazepines

These medications are used to treat symptoms and stop the development of severe withdrawal symptoms, such as seizures and delirium tremens. Titrating the dose according to the patient's response and the severity of symptoms is the aim of treatment; this is frequently done with the help of the CIWA-Ar scale. (Such as diazepam, lorazepam, and chlordiazepoxide)

Barbiturates: In some cases, when benzodiazepines are ineffective, barbiturates like phenobarbital may be used, although their use is less common due to their potential for overdose.

Anticonvulsants (e.g., carbamazepine, gabapentin): These can be used in less severe cases to reduce the risk of seizures and alleviate withdrawal symptoms.

Beta-blockers (e.g., propranolol): Used to manage autonomic symptoms, such as tachycardia and hypertension, which are common in AWS.

Alpha-2 agonists (e.g., clonidine): Can help with autonomic instability, though they are less commonly used.

Supportive Care

Hydration and Electrolyte Replenishment

Many patients with AWS are dehydrated or have electrolyte imbalances, so intravenous fluids and electrolytes may be administered to stabilize them.

Nutritional Support

Chronic alcohol use often leads to deficiencies in vitamins and minerals, particularly thiamine. Thiamine supplementation is essential to prevent Wernicke-Korsakoff syndrome, a severe complication of alcohol use disorder.

Delirium Tremens (DTs)

DTs are the most severe form of alcohol withdrawal and require immediate medical intervention. The management of DTs typically involves high doses of benzodiazepines, often administered intravenously, and intensive monitoring in a hospital setting. The use of thiamine and magnesium sulfate may also be indicated to prevent complications related to alcohol-related neurological damage.

Psychiatric Support

Many individuals undergoing alcohol withdrawal also suffer from anxiety, depression, or other psychiatric conditions. Mental health support, including psychotherapy and medications such as antidepressants or antipsychotics, may be necessary.

Table 1. Alcohol use disorder criteria, as defined by the Diagnostic and Statistical Manual for Mental Disorders, 5th edition (DSM-5) (4), and the International Classification of Diseases, 10th edition (ICD-10) (116).22

ICD-10 criteria for alcohol dependence	DSM-5 criteria for alcohol use disorder
Tolerance	Tolerance
Withdrawal	Withdrawal
Difficulties controlling drinking (unsuccessful in cutting down or stopping drinking)	Difficulties controlling drinking (unsuccessful in cutting down or stopping drinking)
Neglect of activities	Neglect of activities
Time spent drinking or recovering from effects of alcohol	Time spent drinking or recovering from effects of alcohol
Drinking despite physical/ psychological problems	Drinking despite physical/ psychological problems
Craving	Craving
	Alcohol consumed in larger amounts or over longer periods than was intended
	Failure to fulfill major role obligations
	Recurrent alcohol use in hazardous situations
	Drinking despite social/ interpersonal problems

Outpatient Management

In cases of mild withdrawal, outpatient management may be considered. Medications like **carbamazepine or gabapentin** may be prescribed, and patients should be

monitored closely for any progression of symptoms. In patients with a history of mild withdrawal or who have completed a medically supervised detoxification process, outpatient care is feasible. However, patients at higher risk of severe withdrawal should always be treated in an inpatient setting.

Prevention of Alcohol Withdrawal Syndrome [23-24]

The prevention of AWS centers on the management of alcohol use disorder. This includes strategies aimed at reducing or eliminating alcohol consumption over time. Some interventions include:

- **Gradual Reduction:** Slowly tapering alcohol intake to allow the body to adapt and avoid withdrawal.
- **Medications for Alcohol Use Disorder:**

Disulfiram

A medication that causes unpleasant symptoms if alcohol is consumed, deterring alcohol use.

Naltrexone

An opioid antagonist that reduces the pleasurable effects of alcohol, helping to prevent relapse.

Acamprosate

Restores the balance of neurotransmitters affected by alcohol, helping to reduce cravings.

Cognitive Behavioral Therapy (CBT)

This type of therapy focuses on addressing the behaviors and thoughts associated with alcohol use, helping individuals manage triggers and cravings.

Support Groups

Participation in Alcoholics Anonymous (AA) or other peer support groups can provide ongoing support and encouragement in maintaining sobriety.

Recent Advances and Future Directions [25-26]

Recent research has focused on better understanding the pathophysiology of AWS, improving pharmacological treatments, and exploring the role of genetics in alcohol dependence. Future directions include:

Personalized Treatment Plans

Leveraging genetic and phenotypic data to tailor treatment for AWS based on individual characteristics.

Non-Benzodiazepine Therapies

Investigating the role of novel pharmacological agents, such as glutamate antagonists or GABA modulators, to reduce the reliance on benzodiazepines in managing withdrawal.

Digital Interventions

Exploring the potential of mobile apps and online resources to support patients during the withdrawal process and recovery.

Conclusion

Alcohol Withdrawal Syndrome is a complicated illness that necessitates a deep comprehension of its pathophysiology, symptoms, and treatment options. Preventing complications such as seizures, delirium tremens, and death requires early detection and suitable treatment. There is potential for bettering patient outcomes and lessening the burden of alcohol use disorder through ongoing research into more potent treatments and preventative measures.

Disclosure Statement

There are no conflicts of interest.

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